REMARKS

Claims 1 and 8-22 are pending upon entry of the current amendment. Claims 13-22 have been newly added. Support for the foregoing amendment can be found throughout the specification and claims as originally filed, for example, at page 16, line 17 - page 17, line 24; page 74, line 1 - page 88, line 17; page 91, lines 3-8; page 92, lines 10-12; and Table 2. No new matter enters by way of the foregoing amendment.

At the outset, Applicants would like to thank the Examiner for indicating that the claims satisfy the utility requirement under 35 U.S.C. § 101. Office Action at pages 1 and 2. Applicants would also like to thank the Examiner for indicating that Claim 1 is allowable.

I. Claim Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 8-11 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." Office Action at page 2. In rejecting the claims, the Examiner further asserts that "[t]he specification has not disclosed a biological function for the large genus of molecule encompassed by the claims, or otherwise provided guidance with respect to how such molecule may be used." *Id.* At page 4. Applicants disagree.

The Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original).

As the M.P.E.P. makes clear, "(t)he specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." M.P.E.P. § 2164.05(a). *See also*, *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American*

Hoist & Derrick Co., 730 F.2d 1452, 1463 (Fed. Cir. 1984). Furthermore, it is well-established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345 (Fed. Cir. 2000).

Again, Applicants thank the Examiner for indicating that Claim 1, a substantially purified nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 7212 or its complement, is enabled and posses utility. Office Action at pages 1 and 2. Indeed, given the disclosure and the state of the art, one of skill in the art would be able to practice the invention in a manner that is commensurate in scope with the claims without undue experimentation. Given this, Applicants respectfully traverse the Examiner's assertion that nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% identity to SEQ ID: 7212 fail to satisfy the enablement requirement under 35 U.S.C. § 112, first paragraph.

Applicants strongly disagree with the Examiner's assertion that "[t]he skilled artisan would be required to perform unpredictable and undue experimentation to determine how to use nucleic acids which share only a percent identity with the claimed nucleic acid sequence." *Id.* At page 5." This assertion by the Examiner completely disregards the standard of one of ordinary skill in the art. Given at least the teachings of the Specification, one of ordinary skill in the art would have the ability to make nucleotide substitutions to SEQ ID NO: 7212 without undue experimentation. Performing routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976). However, the Examiner ignores this in rejecting claims with a percent identity to SEQ ID NO: 7212, a sequence which the Examiner admits has a well-know and established utility. Office Action at pages 1 and 2.

Further, an analysis of the criteria presented in *In re Wands* supports Applicants' position that no undue experimentation would be required to make and use the claimed invention. *See In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998). Applicants have provided considerable direction and guidance such that it is well within the level of ordinary skill in the art to practice the claimed invention without undue experimentation. For example, the

specification discusses numerous nucleic acid molecules, including SEQ ID NO: 7212 and complement thereof. Specification, for example, at page 15, line 25 - page 20, line 4; page 37 , line 5 - page 42, line 6; and Table 2. Further, the specification provides guidance to one of skill in the art on how to produce transformed plants comprising the disclosed sequences. Specification, for example, at page 15, line 25 - page 20, line 4; page 91, lines 3 - 8; and Example 1. Taken in combination, such disclosure provides adequate direction to those skilled in the art of how to make and use the claimed invention without undue experimentation.

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, expression systems, and enzyme assay conditions, to which a person of ordinary skill in the art has access. One of ordinary skill in the art is sufficiently guided by the Applicants' disclosure, which sets forth nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% identity to SEQ ID NO: 7212. Specification, for example, at page 15, line 25 - page 20, line 4; page 37 , line 5 - page 42, line 6; and Table 2. Further, one of ordinary skill in the art would be sufficiently guided by the Applicants' disclosure, which sets forth numerous plants and host cells capable of being used, without undue experimentation, with the disclosed sequences.

In using the quantity of experimentation factor to reject the claims, the Examiner asserts that "[t]he teaching of the specification and of the prior art do not enable one skilled in the art to use molecules sharing between 90-99% sequence identity with SEQ ID NO: 7212." Office Action at page 4. The Examiner further asserts that "[t]he specification has not disclosed a biological function for the large genus of molecules encompassed by the claims, or otherwise provided guidance with respect to how such molecules may be used." *Id.* Moreover, the Examiner asserts that the percent identity claims are not enabled because "it would be unpredictable for the skilled artisan to determine how to use the nucleic acid sequence which shares homology with the claimed sequence." *Id.* At pages 4-5. Applicants disagree.

This analysis is contrary to the Examiner's own findings regarding SEQ ID NO: 7212. In acknowledging that SEQ ID NO: 7212 satisfies the utility requirement under 35 U.S.C. § 101, the Examiner states that SEQ ID NO: 7212 does not differ from Genbank U50333, a Oryza

sativa gibberellin C-20 oxidase mRNA, "in regions which would likely affect the activity of the enzyme." Office Action at page 2. With this, the Examiner concludes that "it is more likely than not that positions 28575-30173 of SEQ ID NO: 7212 encodes a gibberellin C-20 oxidase." *Id.* Given the Examiner's identification of a critical region and acknowledgement that SEQ ID NO: 7212 would likely encode a gibberellin C-20 oxidase, one of ordinary skill in the art would have the requisite skill to modify SEQ ID NO: 7212 in a manner that is commensurate in scope with the claims without undue experimentation. For example, given the specification, one of skill in the art would recognize that degeneracy of the genetic code would account for nucleic acid molecules comprising different nucleotides but encoding for the same protein with the same function. Specification, for example, at page 39, line 8 - page 40, line 2. Given this, one of skill in the art would recognize that nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% identity to SEQ ID NO: 7212 would have the ability to function as a gibberellin C-20 oxidase.

Moreover, one of skill in the art would also have the ability to modify the nucleic acid sequence of SEQ ID NO: 7212 such that it would encode for a protein with conservative amino acid substitutions. Specification, for example, at page 39, line 20 - page 42, line 6. As provided in the specification, one of skill in the art would recognize that conservative amino acid substitution is based on a variety of well known factors and can be accomplished without undue experimentation. For example, without being limited, one of skill in the art would have the ability to make conservative amino acid substitutions based on the charge, polarity, hydrophobicity, hydrophilicity, and relative side group of the amino acid. *Id.* Additionally, one of skill in the art would recognize that changes to the critical region of a protein should be handled with caution as to avoid influencing the activity of the protein. *Id.* at page 40 , line 16 - page 41, line 3 and page 41, lines 10-15.

In rejecting the claims, the Examiner further asserts that 90% identity to SEQ ID NO: 7212 would encompass 6,900 differences, while 99% identity to SEQ ID NO: 7212 would encompass 690 different nucleotides. Office Action at pages 4-5. The Examiner further assets that changing all 1571 nucleotides in the region of 28575-30173 of SEQ ID NO: 7212 to accommodate the 690 or 6900 nucleotide differences for a nucleic acid molecule that shares 90%

or even 99% identity to SEQ ID NO: 7212 would result in loss of biological function as a gibberellin C-20 oxidase. *Id.* Applicants disagree.

Again, this analysis by the Examiner ignores the fact that one of skill in the art would have the ability to make, without undue experimentation, nucleotide substitutions that would not influence the function of SEQ ID NO: 7212. Further, as confirmed by the art, one of skill in the art would have the knowledge of the critical regions present in SEQ ID NO: 7212 and would have the ability to make substitutions which would not alter the functionality of the protein. Regarding SEQ ID NO: 7212, one skilled in the art has over 69,000 nucleotide choices. As such, contrary to the Examiner's suggestion, one skilled in the art would not change all 1571 nucleotides in the region of 28575-30173 with the expectation of maintaining functionality. Rather, one skilled in the art would have the ability to leave nucleotide positions 28575-30173 unchanged and make nucleotide substitutions in non-critical regions of the protein. In doing so, one of skill in the art could create nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% identity to SEQ ID NO: 7212, with the expectation that the substituted sequence would still function as a gibberellin C-20 oxidase.

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. The specification provides ample guidance such that one of skill in the art would have the ability to practice the invention without undue experimentation. For example, Table 2 identifies positions 28572-20174 of SEQ ID NO: 7212 as a gibberellin C-20 oxidase and positions 28744-29858 of SEQ ID NO: 7212 as a "probable gibberellin C-20 oxidase." Alone, this is sufficient to render the claims enabled. Given the teaching of the specification and the art, one of skill would have the expectation that SEQ ID NO: 7212 would act as a gibberellin C-20 oxidase. Moreover, as set forth above, one of skill in the art would have the ability to make nucleotide substitutions without changing the functionality of the protein.

The fourth, fifth, and sixth *Wands* criteria focus on the nature of the invention, the state of the art, and the relative skill in the art. The specification provides a detailed description of the nucleic acid sequences required by the claims. Specification, for example, at page 15, line 25 -

page 20, line 4; page 37 , line 5 - page 42, line 6; Examples 1-3; and Table 2. Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to generate nucleic acid sequences which are commensurate in scope with the claims.

Regarding the state of the prior art, the Examiner cites to Kang *et al.* (*Plant Physiology*, Vol. 121, page 373-382, 1999) and Perez-Flores *et al.* (*J. of Experimental Botany*, Vol. 54, No. 390, pages 2071-2079, 2003) as evidence of known Gibberellin molecules. Office Action at page 3. The Examiner uses the alignment of the known Gibberellin molecules in the prior art to confirm the utility of SEQ ID NO: 7212. In doing so, the Examiner concludes that "it is more likely than not that positions 28575-30173 of SEQ ID NO: 7212 encodes a gibberellin C-20 oxidase" *Id.* at page 2. Outside of confirming the utility of SEQ ID NO: 7212, the Examiner does not cite to any additional references to support the Examiner's conclusion that nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% to SEQ ID NO: 7212 fail to satisfy the enablement requirement under 25 U.S.C. § 112.

The seventh criterion considers the predictability of the art. Applicants respectfully assert, as discussed *infra*, that the specification discloses sufficient guidance such that a person of ordinary skill in the art would, after reading the specification, have the ability to practice the invention in a manner that is commensurate in scope with the claims. Additionally, the specification provides sufficient guidance such that one of skill in the art would have the ability to make nucleotide substitutions without undue experimentation. Specification, for example, at page 39, line 20 - page 42, line 6. For example, as stated above, one of skill in the art would have the ability to modify the nucleic acid sequence of SEQ ID NO: 7212 such that it would encode for a protein with conservative amino acid substitutions. *Id.* However, the Examiner ignores this factor in rejecting the claims.

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). In the present

case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, methods of modifying nucleic acid sequences sharing between 100% and 90%, between 100% and 95%, between 100% and 98%, and between 100% and 99% to SEQ ID NO: 7212 while still preserving protein function.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

II. Claim Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 8-11 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly "failing to comply with the written description requirement." Office Action at page 7. In rejecting the claims, the Examiner asserts that "[t]he claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention." Office Action at pages 7. Applicants respectfully traverse this rejection.

The purpose of the written description requirement is to ensure that the inventor had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172 (Fed. Cir. 1996). In accordance with this purpose, Applicants need not "describe," in the sense of 35 U.S.C. § 112, all things that are encompassed by the claims. To contend otherwise would contradict established jurisprudence, which teaches that a patent may be infringed by technology developed after a patent issues. *United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251 (Fed. Cir. 1989). A related, and equally well-established principle of patent law is that claims "may be broader than the specific embodiment disclosed in a specification." *Ralston-Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575 (Fed. Cir. 1985), *quoting In re Rasmussen*, 650 F.2d 1212, 1215 (C.C.P.A. 1981). Thus, in order for Applicants to describe each and every molecule encompassed by the claims, it is not required that every aspect of those nucleic acid molecules be disclosed. *In re Alton*, 76 F.3d at 1175 (if a person of ordinary skill in the art would, after reading the specification, understand that the inventors had

possession of the claimed invention, even if not every nuance, then the written description has been met).

An adequate written description of a genus of nucleic acids, such as those recited in claims 8-11, may be achieved by either "a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of genus or of a recitation of structural features common to the members of the genus." *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568-69 (Fed. Cir. 1997). The feature relied upon to describe the claimed genus must be capable of distinguishing members of the claimed genus from non-members. *Id.* Further, Applicants need not describe every possible sequence that may be included in the claimed genus of nucleic acid molecules. Indeed, recently, the Federal Circuit stated that "[i]t is not necessary that every permutation within a generally operable invention be effective in order for an inventor to obtain a generic claim, provided that the effect is sufficiently demonstrated to characterize a generic invention." *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). Applicants have satisfied this requirement.

In rejecting the claims, the Examiner asserts that "[t]he only structural formula given in the specification is SEQ ID NO: 7212" and "[t]he specification discloses only one member of the genus, i.e., SEQ ID NO: 7212." Office Action at pages 9 and 14. The Examiner further asserts that "[f]or all the rejected claims, only a partial structure representing the entire genus is given, that is SEQ ID NO: 7212." The Examiner goes on to assert that "[t]he teachings of the specification do not couple this structure with any additional physical or chemical characteristics." Further, the Examiner asserts that "[t]he specification does not disclose any specific mutant, allelic, or splice variants or homologues of SEQ ID NO: 7212." Office Action at page 12. Applicants disagree.

At the outset, Applicants thank the Examiner for indicating that the specification discloses "one member" of the genus, SEQ ID NO: 7212. Office Action at page 14. Indeed, the specification is replete with structural formulas of SEQ ID NO: 7212. Specification, for example, at Table 2. For example, without being limited, Table 2 identifies over 400 fragments of SEQ ID NO: 7212. Moreover, the function of many of these fragments have been characterized and can be found in Table 2. For instance, Table 2, identifies positions 28572-

20174 of SEQ ID NO: 7212 as a gibberellin C-20 oxidase and positions 28744-29858 of SEQ ID NO: 7212 as a "probable gibberellin C-20 oxidase." However, the Examiner ignores this in rejecting the claims.

Moreover, one of skill in the art would also recognize that Applicants were in possession of a sufficient number of SEQ ID NO: 7212 variants to satisfy the written description requirement under 35 U.S.C. § 112. For instance, given the teachings of the specification, one of skill in the art would have the ability to modify the nucleic acid sequence of SEQ ID NO: 7212 such that it would encode for a protein with conservative amino acid substitutions. Specification, for example, at page 39, line 20 - page 42, line 6. As provided in the specification, one of skill in the art would recognize that conservative amino acid substitution is based on a variety of well known factors and can be accomplished without undue experimentation. For example, one of skill in the art would have the ability to make conservative amino acid substitutions based on the charge, polarity, hydrophobicity, hydrophilicity, and relative side of the amino acid. Moreover, the specification details both the hydropathic amino acid index as well as the hydrophilic value of amino acids. Specification, for example, at page 41, lines 4-26. With this, one of skill in the art would recognize that Applicants were in possession of numerous species of SEQ ID NO: 7212.

In particular, Applicants have disclosed common structural features, for example the nucleotide sequence of SEQ ID NO: 7212. For example, if a particular nucleic acid molecule contains the nucleotide sequence of SEQ ID NO: 7212, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 7212.[1] Moreover, closely related nucleic acid molecules falling within the scope of the claimed invention are readily identifiable - they either contain the nucleic acid sequence of SEQ ID NO: 7212 (or complements or fragments thereof), or share a claimed identity with SEQ ID NO: 7212 (or complements or fragments thereof), or they do not. The fact that the nucleic acid molecules may

[1] The same argument applies with equal force to every genus of the claimed nucleic acid molecules. For example, if a nucleic acid molecule contains a nucleic acid sequence that has 95% identity with SEQ ID NO: 7212, then it is a member of the claimed genus of nucleic acid molecules sharing between 90% and 100% sequence identity with SEQ ID NO: 7212.

comprise additional sequences or variations is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the specification.

In rejecting the claims, the Examiner states that the specification does not disclose a nucleic acid sequence within the genus of nucleic acid molecules having 90 to 99.9% identity with SEQ ID NO: 7212. Office Action at page 14. However, the Examiner has offered no evidence to demonstrate why one of ordinary skill in the art would reasonably doubt that Applicants have adequately described the claimed invention in the present disclosure. Whether or not the genus is large or variable, it shares a common feature, *i.e.*, a substantially purified nucleic acid molecule having the nucleic acid sequence of SEQ ID NO: 7212 or its complement, and one of ordinary skill in the art would recognize that Applicants were in possession of the genus of nucleic acid molecules comprising a nucleic acid sequence having between 100% and 90% identity to the nucleic acid molecule of SEQ ID NO: 7212.

Applicants further disagree with the Examiner's assertion that "[t]he specification does not describe the location or identity of nucleotides which may be varied within SEQ ID NO: 7212, and does not describe the functional activity or other biological role associated with such variants." *Id.* at page 14. Contrary to the Examiner's assertions, the claims do not require "functional" or "biological" activity associated with variants of SEQ ID NO: 7212. As such, the Examiner's assertions regarding "functional" and "biological" lack any legal basis whatsoever.

The fundamental factual inquiry for satisfying the written description requirement is whether the specification conveys with reasonable clarity to those skilled in the art, as of the filing date sought, that Applicants were in possession of the invention as now claimed. *See, e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. *Lockwood*, 107 F.3d at 1572; M.P.E.P. § 2163.02. In light of the disclosure of the specification one of ordinary skill in the art at the time the application was filed would have readily recognized that Applicants were in possession of the invention as claimed.

By describing the common structural feature of the claimed nucleic acid molecules, *i.e.*, SEQ ID NO: 7212, Applicants respectfully submit that they have satisfied, at least, the *Eli Lilly*

test for written description. Therefore, Applicants respectfully request that the Examiner withdraw the rejection of claims 8-11 under 35 U.S.C. § 112, first paragraph.

CONCLUSION

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objection and rejections of the claims, and to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-5243 should any additional information be necessary for allowance.

Respectfully submitted,

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